

REMARKS

Claims 99-177 are pending. Claims 99-113 and 118-123 are under examination. Claims 108, 109 and 126-177 have been canceled. Claims 99, 102, 119, 121 and 123 have been amended. New claims 178-199 have been added. Support for the amendments and new claims can be found throughout the specification and the claims as filed. In particular, support for the amendment to claim 99 can be found, for example, on page 3, lines 4-29, and Examples 1 and 2, pages 67-72. Support for the amendment to claims 102, 119, 121 and 123 can be found, for example, in original claim 1. Support for new claims 178-199 can be found, for example, in original claims 2 and 3 and on page 19, line 28, to page 20, line 2. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested. Entry of the proposed amendments is respectfully submitted to be proper because the amendments are believed to place the claims in condition for allowance.

Applicants appreciate the time and helpful discussion with Examiner Yao and Supervisory Examiner Siew and Applicants' representative in the telephone interview on September 13, 2006. Applicants discussed the written description rejection and possible claim amendments. Applicants believe that the amendment and response reflects the issues discussed during the telephone interview.

The rejection of claims 99-113 and 118-123 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicants respectfully submit that the specification provides sufficient description and guidance for the claimed peptides and conjugates.

During the telephone interview, the claims were discussed with respect to introducing size limitations of the peptides and functional language. The claims have been amended to include both size limitations and functional activity of the peptides. With respect to peptides "comprising" SEQ ID NO:1, Applicants point out, as discussed in the telephone interview, that the specification teaches a peptide "comprising" CREKA (SEQ ID NO:1). In particular, the CREKA (SEQ ID NO:1) peptide was identified using a phage display library that was injected into mice and recovered from breast tumor tissue (Example 1, pages 67-70). A peptide library was used, with the peptide expressed on the surface of the phage as a fusion with a phage

protein, in particular the product of gene III. Such a peptide-gene III fusion protein is exemplary of a peptide “comprising” CREKA (SEQ ID NO:1). During the telephone interview, the question was raised as to the size of the gene III protein as an example of a peptide “comprising” CREKA (SEQ ID NO:1). Submitted herewith as Exhibit 1 is a printout from GenBank of the gene III protein (minor coat protein). The full length protein is 424 amino acids, and the mature protein contains residues 19 to 424, a 406 amino acid protein. Note the title of reference 2 on page 1, “The structural basis of phage display elucidated by the crystal structure of the N-terminal domains of g3p,” indicating that the gene III protein is used as a fusion for phage display.

Regarding the recited size limitations and functional activity, Applicants point out that the claims do not include non-functional variants but only those peptides or conjugates comprising CREKA (SEQ ID NO:1), having a length of less than 100 residues, and that selectively home to tumor vasculature and selectively bind collagen. Therefore, the concerns discussed in the telephone interview of the claims encompassing peptides that do not selectively home to tumor vasculature or selectively bind collagen is not relevant to the claims, as amended, that recite the functional activity of the peptides. Further, the concerns discussed in the telephone interview regarding the possibility that very large peptides “comprising” CREKA (SEQ ID NO:1) may have secondary structure and assume conformations that mask the binding activity of the CREKA (SEQ ID NO:1) sequence are not relevant to the claims, as amended, which require that the largest peptide “comprising” CREKA (SEQ ID NO:1) have a length of less than 100 residues and selectively home to tumor vasculature and selectively bind collagen. Applicants also point out that new claims 178-199 recite increments of smaller peptides than the peptide having a length of less than 100 residues as in claims 99 and 102. Thus, the claims are directed to peptides and conjugates and specifically recite size limitations, having a length of less than 100 residues or shorter recited sizes, and functional activity, selectively homing to tumor vasculature and selectively binding collagen, of the peptides comprising CREKA (SEQ ID NO:1).

Applicants respectfully submit that the specification provides sufficient description and guidance for the claimed peptides and conjugates. Accordingly, Applicants respectfully request that this rejection be withdrawn.

If the Examiner deems the claims to be allowable, Applicants respectfully request that additional species, as recited in withdrawn claims 114-117, 124 and 125, be rejoined since they would include all the limitations of an allowable claim.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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as our correspondence address.**



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Date: September 18, 2006

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Range: from to Features:

1: [P69168](#). Reports Coat protein A pr...[gi:59799327]

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LOCUS P69168 424 aa linear PHG 16-MAY-2006
 DEFINITION Coat protein A precursor (G3P) (Minor coat protein).
 ACCESSION P69168
 VERSION P69168 GI:59799327
 DBSOURCE swissprot: locus COATA_BPM13, accession [P69168](#);
 class: standard.
 extra accessions:P03662,created: Jul 21, 1986.
 sequence updated: Jul 21, 1986.
 annotation updated: May 16, 2006.
 xrefs: [V00604.2](#), [CAA23862.1](#), [Z3BPM3](#), [1G3P_@](#), [1TOLA](#)
 xrefs (non-sequence databases): LinkHub:P69168, InterPro:IPR008021,
 Pfam:PF05357
 KEYWORDS 3D-structure; Capsid protein; Phage recognition; Signal; Virion
 protein.
 SOURCE Enterobacteria phage M13
 ORGANISM [Enterobacteria phage M13](#)
 Viruses; ssDNA viruses; Inoviridae; Inovirus.
 REFERENCE 1 (residues 1 to 424)
 AUTHORS van Wezenbeek,P.M., Hulsebos,T.J. and Schoenmakers,J.G.
 TITLE Nucleotide sequence of the filamentous bacteriophage M13 DNA
 genome: comparison with phage fd
 JOURNAL Gene 11 (1-2), 129-148 (1980)
 PUBMED 6254849
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA].
 REFERENCE 2 (residues 1 to 424)
 AUTHORS Lubkowski,J., Hennecke,F., Pluckthun,A. and Wlodawer,A.
 TITLE The structural basis of phage display elucidated by the crystal
 structure of the N-terminal domains of g3p
 JOURNAL Nat. Struct. Biol. 5 (2), 140-147 (1998)
 PUBMED 9461080
 REMARK X-RAY CRYSTALLOGRAPHY (1.46 ANGSTROMS) OF 19-235.
 REFERENCE 3 (residues 1 to 424)
 AUTHORS Lubkowski,J., Hennecke,F., Pluckthun,A. and Wlodawer,A.
 TITLE Filamentous phage infection: crystal structure of g3p in complex
 with its coreceptor, the C-terminal domain of TolA
 JOURNAL Structure 7 (6), 711-722 (1999)
 PUBMED 10404600
 REMARK X-RAY CRYSTALLOGRAPHY (1.85 ANGSTROMS) OF 19-105 OF COMPLEX WITH
 TOLA.
 COMMENT On or before May 27, 2005 this sequence version replaced gi:[75781](#),
 gi:[116661](#).
 [FUNCTION] Coat protein A is necessary for adsorption of the virion
 onto the F-pilus of the host cell.

EXHIBIT 1

[SUBUNIT] There are about five copies of this protein per mature phage.

[DOMAIN] Consists of three domains (N1, N2, and CT). The N2 domain interacts with the F pilus, whereas the N1 domain (connected to N2 by a flexible glycine-rich linker and tightly interacting with it on the phage) forms a complex with the C-terminal domain of tolA at later stages of the infection process.

[MISCELLANEOUS] They are located at the adsorption end of the phage particle.

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<u>Protein</u>	1..424 /gene="III" /product="Coat protein A precursor"
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ORIGIN

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121 inpldgtypp gteqnpapn psleesqpln tfmfqnnrfr nrqgaltvyt gtvttgtdpv
181 ktyyqytpvs skamydaywn gkfrdcafhs gfndpfvce yggqssdlpq ppvnagggsg
241 gsggggsegg gsegggsegg gseggsggg sgsgdfdyek manankgamt enadenalqs
301 dakgklsva tdygaaidgf igdvsglang ngatgdfags nsqmaqvgdg dnsplmnnfr
361 qylpslpqsv ecrpfvfsag kpyefsidcd kinlfrgvfa fllyvatfmy vfstfanilr
421 nkes
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